REMARKS

This is intended as a full and complete response to the Office Action dated February 3, 2009, having a shortened statutory period for response extended two months and set to expire on July 6, 2009. Please reconsider the claims pending in the application for reasons discussed below.

Claims 23-43 are pending in the application. Claims 23-33 remain pending following entry of this response. Claims 23 and 30 have been amended. Claims 34-43 have been canceled. Applicants submit that the amendments do not introduce new matter.

Further, Applicants are not conceding in this application that those amended or canceled claims are not patentable over the art cited by the Examiner, as the present claim amendments and cancellations are only for facilitating expeditious prosecution of the claimed subject matter. Applicants respectfully reserve the right to pursue these pre-amended or canceled claims and other claims in one or more continuations and/or divisional patent applications.

Election/Restriction

Applicants confirm the election of Group I (claims 23-33) for examination. The election is made without traverse.

Specification Objections

The Examiner objects to the use of an acronym in the title, CS. Applicants have amended the title to define the acronym "CS" as "Core-Shell," thereby obviating this objection. Withdrawal of this objection is respectfully requested.

Claim Rejections - 35 U.S.C. § 112

Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse this rejection, but have amended claim 30 to be more definite, thereby obviating this rejection. Withdrawal of the rejection is respectfully requested.

Claim Rejections - 35 U.S.C. § 103

Claims 23-29 and 31-33 are rejected under 35 U.S.C. § 103(a) as being unpatentable over *Decher et al.* ("Multilayer Thin Films, hereinafter, "*Decher*") in view of *Walt et al.* (U.S. Publication 2002/0172716, hereinafter, "*Walt*").

Applicants respectfully traverse this rejection.

The Examiner bears the initial burden of establishing a *prima facie* case of obviousness. See MPEP § 2141. Establishing a *prima facie* case of obviousness begins with first resolving the factual inquiries of *Graham v. John Deere Co.*, 383 U.S. 1 (1966). The factual inquiries are as follows:

(A) determining the scope and content of the prior art;
(B) ascertaining the differences between the claimed invention and the prior art;
(C) resolving the level of ordinary skill in the art; and
(D) considering any objective indicia of nonobviousness.

Once the *Graham* factual inquiries are resolved, the Examiner must determine whether the claimed invention would have been obvious to one of ordinary skill in the art.

Respectfully, Applicants submit that the Examiner has not properly characterized the teachings of the references and/or the claims at issue. Accordingly, a *prima facie* case of obviousness has not been established.

For example, the Examiner relies on *Decher* in view of *Walt* as teaching preparing of porous templates as recited in claim 23. However, *Decher* discloses formation of LbL-shells on templates, but does not disclose the use of porous templates. LbL formation includes adsorption of alternately charged polyelectrolytes or nanoparticles on a surface. This results in a layered shell structure.

Completely different thereto is the approach by *Walt* who describes two processes:

- "A method for preparing a core-shell composite includes the following steps: providing a microsphere substrate; contacting the microsphere substrate with a

polymer nanosphere to yield a colloidal assembly; and heating the assembly to yield a core-shell composite" (*Walt*, page 2, paragraph [0015] and page 13, claims 29 and 40), wherein "the colloidal assembly is heated to a temperature greater than the T_g of the polymer nanosphere(s) to melt the polymer nanospheres" (*Walt*, page 2, paragraph [0018]).

- "The invention also includes methods of making hollow microspheres by providing a substrate containing a plurality of hydroxyl groups and attaching an initiator agent to the hydroxyl groups to form attached initiator agents. Any solid substrate, which is characterized as containing hydroxyl groups on its surface and is dissolvable (following polymerization of the shell), is suitable" (*Walt*, page 1, paragraph [0012] and claim 23). The shell is therefore formed by *living radical polymerization* (*Walt*, paragraphs [0003]-[0041]).

Evidently, the first process described by *Walt* includes *heating* a colloidal assembly to a temperature above T_g of the polymer *to generate a shell by melting*. This process is completely different from *Decher's* LbL technology since no alternately charged polyelectrolyte *layers* (plural) are adsorbed to a substrate.

The second process described by *Walt* requires a substrate containing a plurality of hydroxyl groups for crosslinking an initiator agent thereto. The shell is therefore formed by polymerization. The initiator agent is covalently bound by *Walt* different than the electrostatic attraction used to form LbL shells. *Walt* does not even use the technical term "polyelectrolyte."

Since *Walt* uses—in comparison to *Decher*—completely different approaches to form a shell, a person skilled in the art would not consider combining *Walt* with *Decher*.

Furthermore, *Walt* does not disclose porous templates and, therefore, fails to overcome the deficiencies in *Decher*. In connection with this, the Examiner refers to page 1, paragraph [0007] of *Walt*. However, this paragraph reads

> The microspheres contain pores. A pore is a void *in the polymeric shell* through which a composition may gain access to the hollow portion of the microsphere. The microspheres have certain porosity, and the porosity is varied depending on the size and composition of the substrate used to make the sphere. Pore size is varied depending on the size and nature of the composition to be loaded into the hollow center of the sphere as well as by changing the amount of crosslinking agent added during polymerization. For example, the addition of increasing amounts of a crosslinking agent produces microspheres with decreasing pore size. Pore size is also affected by the addition of a foaming agent, i.e., addition of a foaming agent during production of the shell increases pore size. For example, a pore has a diameter in the range of 10-500 nm.

Clearly, *Walt's* shell, and not the core, includes pores. The *porosity of the shell* can be varied during shell formation of *Walt* (paragraph [0007]).

In addition, *Decher* does not describe that an active compound is adsorbed in a porous template. Applicants respectfully submit that the Examiner misinterprets the statement of *Decher* (page 5, Fig. 1.4) that proteins can be used in layer-by-layer deposition (page 11, 2nd paragraph of the current Office Action). The legend to the cited Figure 4 reads:

> Reagents for layer-by-layer *deposition*…One should also note that small molecules and complex ions are sometimes more difficult to incorporate *into multilayer films* in a regular way than, for example, charged macromolecules.

Layer-by-layer deposition as well as incorporation into multilayer films is not "adsorbing in the porous templates…" as recited in claim 23 of the present application.

Moreover, Applicants respectfully submit that the "incorporation of enzyme crystals and low molecular weight dyes" as alleged by the Examiner is first an incorrect citation, since it relates to "colloid cores [which] can be varied from enzyme crystals to *crystallized* low molecular weight dyes…" Hence, *Decher* describes that crystals can be used as templates on which shells are subsequently formed.

Second, a crystal of an active compound provided to be subsequently encapsulated by an LbL-shell does not represent an entity *adsorbed in* a porous template. The crystal itself forms the template in *Decher*, but is not adsorbed in a porous template. Furthermore, there is no suggestion

by *Decher* to encapsulate proteins or enzymes by their prior adsorption insides pores of a porous template.

With respect to the adsorption of an active compound in to a porous template, the Examiner refers to page 2, paragraph [0017] of *Walt* and alleges that "the microsphere (i.e. template) contains biotin or avidin." Paragraph [0017] merely describes that the microsphere can be "optionally modified to contain a *reactive* substituent." With respect to biotin, paragraph [0017] describes that "the nanosphere contains avidin and the microsphere contains biotin, or the nanosphere contains biotin and the microsphere contains avidin." Nanospheres are assembled *onto* the surface of the microsphere (*Walt*, page 2, paragraph [0016]). No indication is given that a compound is incorporated into a porous template.

Furthermore, *Decher* in view of *Walt* does not teach, show, or suggest "applying at least one primer layer to the porous templates" as recited in independent claim 23. The Examiner alleges that *Walt* describes a stabilized polymer layer which is comparable to a primer layer of the present application. The Examiner apparently considers the formation of a core-shell composition that "comprises nanospheres comprising an amine-modified polystyrene and a microsphere comprising glutaraldehyde-activated silica" to be comparable to a primer layer which is formed by an extra crosslinking step as described on page 14, paragraph 3, lines 8-11 of the present application. Applicants respectfully disagree.

It should be noted that claim 23 defines the material of the primer layer which is selected such that the pores of the porous templates are closed and that the primer layer is largely impermeable to the coating materials applied in the formation of the capsule shell.

Walt merely forms a *single* layer on microspheres. Hence, no primer layer is formed onto which alternately charged polyelectrolytes or alternately charged nanoparticles are coated to form a multilayer shell. Consequently, *Walt* cannot describe that the material used to form the shell is selected to prevent permeation of a coating material. In connection with this, it should be noted that *Walt's* polymeric shell includes *pores* as explicitly stated in paragraph [007] on page 1. *Walt's* polymeric shell would therefore be permeable to coating material.

Moreover, *Walt* melts the nanospheres assembled onto the microsphere. Crosslinking may occur between the nanospheres (amine-modified polystyrene) and the microsphere (glutaraldehyde-activated silica). This is different from what is described in the present application on page 14. Third paragraph of the application describes an extra crosslinking step of amino-functionalized polyelectrolytes. This results in a crosslinking between the polyelectrolytes of the primer layer (*i.e.*, *within the primer layer*). *Walt* crosslinks the nanospheres, which subsequently form the polymer shell, with the microsphere. This results in a crosslinking *between shell and core*. Hence, *Walt* describes a different structure than the present application. Consequently, the properties are different and cannot be expected to be the same.

In addition to that, as being evident for a person skilled in the art, any layer of melted particles will be different from a primer layer of *non-molten* material.

Finally, since no porous templates are used by *Walt*, *Walt* also fails to disclose selecting the material such that the pores are closed.

Turning to *Decher*, only the importance of a strong adsorption of the first layer to anchor the first polymer is described (chapter 3, page 94, paragraph 1, lines 8-12). However, no suggestion is given that this first layer shall close any pores and be impermeable for subsequently deposited coating material. Having a strong adsorption is a different object than closing pores and being impermeable. Consequently, a person skilled in the art cannot derive anything which would lead him to the specific needs of the primer layer as defined in claim 23.

Therefore, a person skilled in the art cannot derive from *Decher* or *Walt*, alone or in combination, neither explicitly or implicitly, any information regarding porous templates and encapsulation of an active compound therein and how to make a suitable primer layer, which: (1) closes pores of the porous templates; and (2) is largely impermeable to the coating materials applied in the formation of the capsule shell.

Accordingly, Applicants submit that claim 23, as well as claims dependent therefrom, are allowable and respectfully request withdrawal of this rejection.

Double Patenting Rejection

The Examiner is aware of U.S. Patent Application Serial No. 10/522,998 with the inventive entity of Lars Dahne, Barbara Baude, and Andreas Voigt. The Examiner is aware of U.S. Patent Application Serial No. 10/535,714 with the inventive entity of Andreas Voigt and Lars Dahne.

Applicants acknowledge the double patenting rejections and respectfully request that the rejections be held in abeyance because (i) no claim in the present application is currently allowable and (ii) the applications on which the rejections are made have not issued. Because it is possible that no claims will issue, or that the claims of the present application will be amended in such a way to overcome the Examiner's concerns regarding double patenting, Applicants defer responding until the present rejection ripens into an actual double patenting rejection.

Conclusion

Having addressed all issues set out in the office action, Applicants respectfully submit that the claims are in condition for allowance and respectfully request that the claims be allowed.

Dated: July 6, 2009

Respectfully submitted, and
S-signed pursuant to 37 C.F.R. 1.4,

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